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TRANSMITTAL LETTER (General - Patent Pending)	Docket No. BDA-0038

In Re Application Of: **Roger S. Cubicciotti**

Serial No.	Filing Date	Examiner	Group Art Unit
09/171,885	October 28, 2998	Lakshmi S. Channavajjala	1615

Title: **PRODRUG COMPOSITIONS AND DRUG DELIVERY METHODS USING SYNTHETIC RECEPTORS**

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Reply Brief

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Kathleen A. Tyrrell

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Dated: **April 26, 2004**

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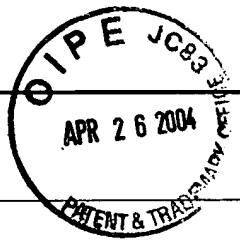
CERTIFICATE OF MAILING BY "EXPRESS MAIL" (37 CFR 1.10) Applicant(s): **Roger S. Cubicciotti**			Docket No. **BDA-0038**
Serial No. **09/171,885**	Filing Date **October 28, 1998**	Examiner **Lakshmi S. Channavajjala**	Group Art Unit **1615**

Invention: **PRODRUG COMPOSITIONS AND DRUG DELIVERY METHODS USING SYNTHETIC RECEPTORS**



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35/Reply Brief (3)

Attorney Docket No.:	**BDA-0038**
Inventors:	**Roger S. Cubicciotti**
Serial No.:	**09/171,885**
Filing Date:	**October 28, 1998**
Examiner:	**Channavajjala, Lakshmi Sarada**
Group Art Unit:	**1615**
Title:	**Prodrug Compositions and Drug Delivery Methods Using Synthetic Receptors**

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By Kathleen A. Tyrrell
Typed Name: **KATHLEEN A. TYRRELL, Reg. No. 38,350**

Mail Stop AF
Commissioner for Patents
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Dear Sir:

REPLY BRIEF

Table of Contents

This reply brief is being filed in accordance with 37 § C.F.R. 1.193(b)(1) in response to the Examiner's Answer dated February 24, 2004 to address certain issues raised in the Examiner's Answer.

I. Status of Rejections

The Examiner has withdrawn the rejection of claims 36, 39 and 40 under 35 U.S.C. § 102(b) as being anticipated by Morgan Jr. et al. (U.S. Patent 5,106,951) and the rejection of claims 34, 35, 37 and 38 under 35 U.S.C. § 103(a) as being obvious over Morgan Jr. et al. (U.S. Patent 5,106,951). However, the Examiner has maintained the rejection of claims 34, 35, 37 and 38 as being unpatentable under 35 U.S.C. § 102(b) as being anticipated by Morgan Jr. et al. (U.S. Patent No, 5,160,951). Further, the Examiner has maintained the rejection of claims 36, 39 and 40 under 35 U.S.C. § 103(a) as being obvious in light of Morgan Jr. et al. (U.S. Patent 5,106,951).

II. Revised Grouping of Claims

In light of the withdrawal of the rejection of claims 36, 39 and 40 under 35 U.S.C. § 102(b) and the rejection of claims 34, 35, 37 and 38 under 35 U.S.C. § 103(a) in the Examiner's Answer, Appellant has revised the grouping of the claims.

Claims 34, 35, 37 and 38 stand or fall together on the issue of novelty under 35 U.S.C. 102(b).

Claims 36, 39 and 40 stand or fall together on the issue of obviousness under 35 U.S.C. 103(a).

III. Arguments

Appellant respectfully traverses the rejection of claims 34, 35, 37 and 38 as being unpatentable under 35 U.S.C. § 102(b) as being anticipated by Morgan Jr. et al. (U.S. Patent 5,160,951).

Appellant respectfully traverses the rejection of claims 36, 39 and 40 under 35 U.S.C. § 103(a) as being obvious in light of Morgan Jr. et al. (U.S. Patent 5,106,951).

A. Inconsistent descriptions of how the teachings of Morgan Jr. et al. relate to an "antibody fragment" are provided by the Examiner

The primary controversy between Appellant and the Examiner in these rejections under § 102(b) and 103(a) resides in whether or not Morgan Jr. et al. teaches the embodiment of the present invention where the synthetic receptor is an antibody fragment.

Appellant does not believe that the teachings of Morgan Jr. et al. anticipate or render obvious embodiments of the present invention wherein the synthetic receptor is an antibody fragment.

Further, controversy appears to exist with the Examiner regarding how Morgan Jr. et al. allegedly teaches embodiments wherein the synthetic receptor is an antibody fragment. Within the single document of the Examiner's Answer, inconsistent positions are taken by the Examiner with respect to how the

teachings of the '951 patent meet the limitation of antibody fragment. In particular, at page 4 of the Examiner's Answer the Examiner "takes the position that the **antibody csDBM complex** (emphasis added) of '951 is considered an antibody fragment that makes up the synthetic receptor." On page 6-7, however, the Examiner suggests that despite the fact that Morgan Jr. et al. does not use the term antibody fragment, the teaching of oligopeptides that constitute **csDBM** reads [on] antibody fragments because antibodies are made up of peptides and oligopeptides. Further on page 7, the Examiner suggests that given their plain meaning the antibody fragment includes oligopeptides and thus reads on **csDBM** of Morgan Jr. et al.

In contrast, Appellant has consistently made clear what he considers the term "antibody fragment" to mean. Appellant has placed evidence on the record in support of this definition. Further, Appellant's definition of "antibody fragment" is consistent with teachings at col. 7, lines 12-15 of Morgan Jr. et al. regarding antibody fragments.

Thus, all evidence of record clearly and consistently distinguishes embodiments of the present invention wherein the synthetic receptor is an antibody fragment from either the csDBM or the antibody csDBM complex of Morgan Jr. et al.

B. The Examiner's interpretation of the term antibody fragment is far broader than reasonably allowed

Appellant understands that during examination the claims must be interpreted as broadly as their terms reasonably allow. However, the MPEP and the Courts are quite clear; when not defined by applicant in the specification, the words of a claim must be given their plain meaning. In other words, they must be read as they would be interpreted by those of ordinary skill in the art. MPEP § 2111.01 and *Rexnord Corp. v. Laitram Corp.* 274 F.3d 1336, 1342, 60 USPQ2d 1851, 1854 (Fed. Cir. 2001).

At page 6 of the Examiner's Answer, the Examiner suggests that in the absence of a definition for "antibody fragment" in the specification, an antibody is nothing but a protein (polypeptide) and an antibody fragment includes peptide fragments.

The Examiner's interpretation of the term "antibody fragment" is unreasonably broad, unsupported by any evidence, and contradictory to evidence of record including Morgan Jr. et al. which makes clear at col. 7, lines 12-15, what the term antibody fragment means. Also see Section VIII (A)(5) of the Appeal Brief for a detailed description of the plain meaning of the term antibody fragment by others skilled in the art.

C. Examiner's characterization of Morgan Jr. et al. is not based upon its teachings as whole

It is respectfully pointed out that a number of statements in the Examiner's Answer regarding teachings of Morgan Jr. et al. are either incorrect or incomplete.

For example, at page 6, the Examiner states that Morgan Jr. et al. does not use the term antibody fragment. This is incorrect. Morgan Jr et al. explicitly uses the term "antibody fragments" at col. 7, lines 12-15 wherein it is taught that "[e]xamples of targeting proteins include antibodies, antibody fragments (Fab, $F(ab)^2$, and Fab'), monoclonal antibodies . . ."

Further, the Examiner's suggestion at page 4 of the Examiner's Answer is based upon an incomplete quote. The Examiner suggests that the teachings at column 5, lines 11-17 of Morgan Jr. et al. which disclose that the "csDBM is specifically designed to fit the drug molecule and undergo multiple non-covalent interactions with a drug" meet the limitations of the instant claimed invention which recites that the drug is specifically bound to the synthetic receptor via non-covalent interactions between the selected drug and the synthetic receptor.

The entire section at col. 5 lines 11-17 reads as follows:

> The present invention provides for a csDBM that is specifically designed to fit the drug molecule to enhance its binding affinity to antibody or carrier and to provide a conjugate stable enough to arrive at target sites with most of the drug still bound.

When read in its entirety, this section makes clear that Morgan Jr. et al. requires a csDBM to link the drug molecules to the carrier or antibody. Such a linking molecule is not required with the synthetic receptors of the present invention.

Also incomplete is the characterization of teachings at col. 10, lines 3-9 regarding aromatic or charged amino acids of an antibody or a protein such as albumin forming a csDBM structure that is capable of binding the drug moiety. The entire section reads as follows:

> Under certain conditions, an appropriate juxtaposition of aromatic as well as charged amino acid residues may occur in an antibody or carrier protein like albumin, that may form a csDBM structure capable of binding, such that only the dehydrating agent need be used to initiate the reactions. However, drugs with such a high degree of interaction with a protein are uncommon.

When read in its entirety, this section also makes clear that Morgan Jr. et al. requires a csDBM to link the drug molecules to the carrier or antibody. Such a linking molecule is not required with the synthetic receptors of the present invention.

MPEP 2141.01 is clear; ascertaining the differences between the prior art and the claims at issue requires interpreting the

claim language and considering both the invention and the prior art references as a whole. Further, MPEP 2141.03 states that the prior art must be considered in its entirety, including disclosures that teach away from the instant invention.

Clearly, the definition in Morgan Jr. et al. of the term "antibody fragment" at col. 7, lines 12-15 not inclusive of the csDBM or antibody csDBM complex of Morgan Jr. et al., teaches away from any interpretation that the csDBM or antibody csDBM complex is considered an "antibody fragment".

Further, all teachings of Morgan Jr. et al., when read in their entirety, make clear that a csDBM is a required element of Morgan Jr et al. to link the drug to a carrier or antibody.

D. The prior art cannot anticipate the claim if there is any structural difference

At page 5-6 of the Examiner's answer, the Examiner states that "Applicant's arguments are not found persuasive because admittedly the csDBM of Morgan Jr. et al. binds to the drug moiety via a non-covalent fashion and applicants do not claim the argued features of csDBM such as the form of csDBM". It is respectfully pointed out, however, that Appellant does not claim the csDBM because the invention does not require a csDBM for its function.

MPEP § 2114 is clear; even if a prior art device performs all the functions recited in the claim, the prior art cannot anticipate the claim if there is any structural difference.

It is unclear to Appellant how the absence of this required element of Morgan Jr. et al. in the instant claimed invention in any way renders arguments presented in the Appeal Brief "unpersuasive."

Instead, the fact that "applicants do not claim the argued features of a csDBM such as the form of the csDBM" renders the claimed invention novel and unobvious over Morgan Jr. et al. as there are clearly structural differences between the claimed invention and the teachings of Morgan Jr. et al.

E. Clarification of Argument presented in Section VIII(A)(5) of Appeal Brief

The Examiner suggests at page 7 of the Examiner's Answer that arguments that the interpretation of the antibody-csDBM of Morgan Jr. et al. to meet the "antibody fragment" limitation of claims 34, 35, 36, 37, 38, 39 and 40 is inconsistent with teachings in Morgan Jr. et al. of embodiments involving a conjugate comprising an antibody fragment as the targeting protein, a csDBM moiety, and a drug (exemplified at col. 4, lines 61-67, of Morgan Jr. et al.) were "persuasive because the instant claim does not exclude the presence of an antibody along with an antibody fragment". Since the rejection was maintained Appellant

believes that the Examiner meant to suggest that the arguments were "unpersuasive." Further, it appears from the Examiner's comment that the argument was misunderstood. This argument was presented as further evidence of the unreasonably broad interpretation by the Examiner of the term "antibody fragment" to include a csDBM and is unrelated to whether or not the instant claimed invention can encompass embodiments with an antibody and an antibody fragment. The point made by this section of the Appeal Brief was that if Morgan Jr. et al. considered the term antibody fragment to include csDBM, binding of the csDBM moiety to an antibody fragment would not be taught by Morgan Jr. et al.

IV. Conclusion

The Examiner's suggestion that Morgan Jr. et al. anticipate or render obvious the instant claimed invention is based upon an unreasonably broad definition of the term "antibody fragment" inconsistent with prior art of record including Morgan Jr. et al., a failure to consider the teachings of Morgan Jr. et al. in their entirety, and a failure to appreciate the significance of structural differences between the instant claimed invention and the teachings of Morgan Jr. et al. with respect to the novelty and unobviousness of the instant claimed invention. Reconsideration and withdrawal of the pending rejections of

claims 34, 35, 36, 37, 38, 39 and 40 under 35 U.S.C. 102(b) and 103(a) is therefore respectfully requested.

Respectfully submitted,

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Date: **April 26, 2004**

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